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The time factor in fetal distress

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It is obviously clinically impossible to establish **how long a fetus in distress can survive** except in the few recognized cases where death occurs before delivery is achieved. It is therefore an advantage to resort to theoretical calculations which give good information about the time factor in fetal hypoxia. It will also be shown from scalp blood measurements that the degree of oxygen deficiency may be estimated.

1. Hypoxia — hypoxemia

Terminology is uninteresting to most readers, but it must be stated that hypoxia and hypoxemia are different terms, unfortunately often confused. **Hypoxia signifies a true tissue oxygen deficiency,** i. e. the tissues have less oxygen than is needed per unit of time and this results in lactic acid production. Hypoxemia is a lower than normal oxygen saturation or oxygen tension in the blood, and pronounced hypoxia is usually present. **Hypoxemia refers only to the blood and is determined by the oxygen saturation or tension, whereas hypoxia refers to the tissues and is usually determined by pH, base deficit, or lactic acid concentration** of plasma or blood.

2. Oxygen and carbohydrate stores for utilization during reduced oxygen supply

If the oxygen supply is reduced below its consumption the fetus may utilize its oxygen stores and/or supply the caloric requirements by the anaerobic breakdown of glycogen to glucose and lactic acid. **The survival time during oxygen deficiency is therefore dependent upon the size and sum of the oxygen and carbohydrate stores.** As most oxygen is stored in hemoglobin it suffices to consider the **oxygen content of the red cells,** and as most carbohydrate is stored in the form of glycogen, the anaerobic stores are assumed to be the **glycogen content of the fetus.** It is assumed that the fetal metabolic rate is constant.

Curriculum vitae

GÖSTA ROOTH *was born in Stockholm in 1918 and went to school there. He entered the University of Uppsala in 1938 and moved to the University of Lund in the same year. He qualified as a Physician in 1945, and submitted his thesis for M. D. in 1949. In 1957 he became Assistant Professor, and in 1966 Research Professor of medicine and has had an appointment at the Department of Medicine. From an interest in respiratory physiology he began to study the fetal respiration in the middle of 1950 and has since mainly worked with perinatal problems. Several of his studies have dealt with the interaction of maternal and fetal acid-base balance. Besides his scientific papers he has written two short textbooks on acid-base and electrolyte balance. Current studies deal with the fetal metabolism during labor.*

2.1 The oxygen stores

Assuming that the oxygen consumption is 8 ml O_2/min/kg (CRENSHAW, HUCKABEE and CURET [2]), that the initial mean oxygen saturation is 50 per cent, that the hemoglobin concentration is 16 g/100 ml of blood, that the fetal weight is 3 kg, and that its blood volume is 350 ml (SMITH [9]), we then have:

Fetal oxygen consumption = 24 ml/min

Fetal oxygen stores = $16/100 \times 1.3 \times 50/100 \times 350 = 36$ ml (as 1 g of hemoglobin binds 1.3 ml of O_2).

Let us first calculate the effect of an apparently small oxygen deficit. If we assume that the fetus obtains 96 per cent of its oxygen consumption, it

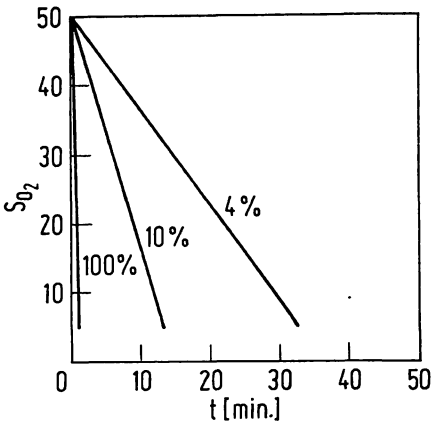

Fig. 1. Change in fetal oxygen saturation (in per cent) at different levels of oxygen deficiency

then has an oxygen deficit of 4 per cent, but such a small deficit can hardly be measured with confidence even experimentally. A 4 per cent deficit = 4/100 × 24 ml/min or 1 ml/min. It follows that in 18 minutes half the oxygen and in 36 minutes all the oxygen is used. Even if the figure for the oxygen consumption were only half of the assumed 8 ml/min/kg, which is unlikely, the oxygen stores would not last for more than about one hour. Fig. 1 illustrates the speed with which the oxygen stores are depleted at various oxygen deficiencies including 100 per cent (for instance with total occlusion of the cord).

2.2 The glycogen stores

To the time in fig. 1 should be added the survival time provided by the glycogen stores. The latter are given as 11 g/kg (Dawes and Shelley [3]) or 33 g in our case. These 33 grams of glycogen give 33 grams of glucose. With oxygen this would

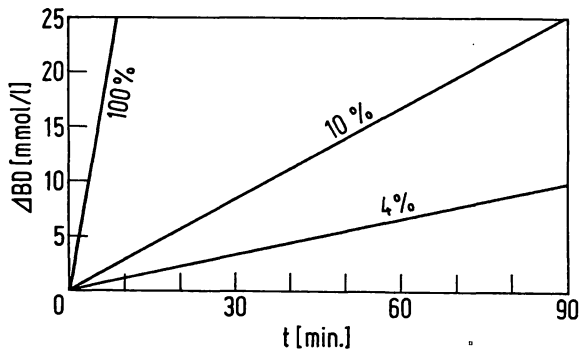

Fig. 2. Changes in fetal base deficit at different levels of oxygen deficiency

give 33 × 4 = 132 kcal, but anaerobically only 1/19 or 7 kcal is obtained. An oxygen consumption of 8 ml/min/kg corresponds to a production of 0.04 kcal/min/kg or 0.12 kcal/min in our example, as 4.9 kcal are produced per liter of oxygen. The deficit was assumed to be 4 per cent or 0.12 × 4/100 = 0.48/100 kcal/min or in 10 minutes 0.048 kcal. With such a small deficit the calories in the glycogen stores last much longer than the oxygen stores (fig. 2). If the pH did not fall enough to inhibit further metabolism the **glycogen stores would last about 60 minutes during total oxygen deprivation.**

2.3 How does glucose breakdown affect fetal scalp blood pH?

33 grams of glucose equals 183 mmol. During breakdown of 1 mmol of glucose 2 mmol of lactic acid are produced. In our case, the total breakdown of the glycogen would give 366 mmol and, as mentioned above, this gives about 7 kcal, i. e. 50 mmol H^+/kcal.

In the previous example, a 4 per cent or 1 ml/min deficiency in oxygen supply corresponds to a deficit of 5/1000 kcal/min. It follows that in 20 minutes the deficit is 0.1 kcal and this produces 5.0 mmol H^+. The hydrogen ions are liberated in the tissues, but some of them appear rapidly in the extracellular fluid. If we assume that the hydrogen ions produced are evenly distributed throughout the body water, taken as 70 per cent of the weight (Smith [9]), and that the intra- and extracellular fluid volumes are about equal, the mean base deficit of the extracellular fluid increases 2.5 mmol/l in 20 minutes. In itself this would decrease pH by 0.05 pH units. However, the CO_2 liberated when the lactic acid is added to the body fluids probably cannot diffuse to the maternal circulation at all and we must therefore assume that the total body CO_2 content remains the same. If no major shifts of CO_2 occur between the intra- and extracellular fluid compartments, the CO_2 content of the plasma may be used as an approximation of the total CO_2 content of the extracellular fluid. With initial values pH 7.36, P_{CO_2} 38 mm Hg, BD_{ECF} 3.5 mmol/l, and total CO_2 of plasma 21.8 mmol/l, this increase of 2.5 mmol/l in BD_{ECF} will give the following result: pH 7.29 and P_{CO_2} 44 mm Hg.

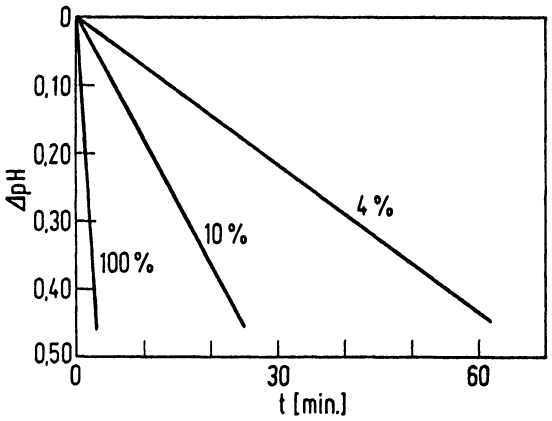

Fig. 3. Changes in fetal pH at different levels of oxygen deficiency

Fig. 3 shows the calculated pH drop with time, assuming as before a 4, 10 and 100 per cent oxygen deficiency.

2.4 Simultaneous use of the oxygen and glycogen stores

In actual fact, during oxygen deficiency there is a fall both in pH and oxygen saturation of the fetal scalp blood. Rooth, McBride and Ivy [6] found that the **oxygen saturation of the fetal scalp blood dropped 28 per cent when the pH dropped 0.10 pH units.** Calculating the caloric equivalent as above it is found that the oxygen saturation decrease corresponds to 100 kcal and the anaerobic metabolism to another 60 kcal. This would indicate that about **60 per cent of the oxygen deficit is drawn from oxygen stores and the rest from anoxic metabolism.**
If we now assume this observed relation between the aerobic and anaerobic metabolism, the changes in pH and oxygen saturation with time are shown

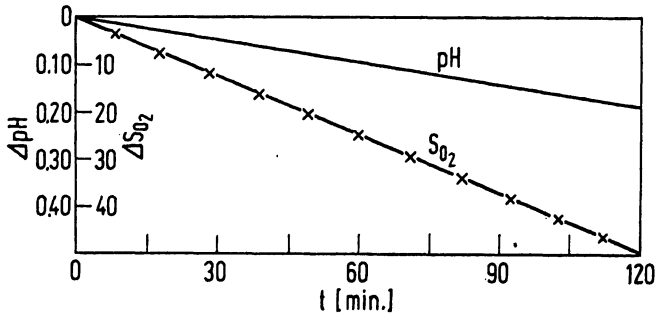

Fig. 4. Changes in fetal pH and oxygen saturation (per cent) with time when 60 per cent of the energy is derived from aerobic and 40 per cent from anaerobic metabolism and when there is a 2 per cent oxygen deficiency

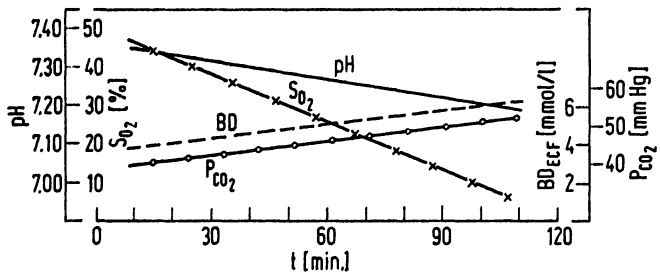

Fig. 5. Same premisses as in fig. 4. Actual values for fetal pH, S_{O_2}, BD, and P_{CO_2} at a 2 per cent oxygen deficiency after initially normal values

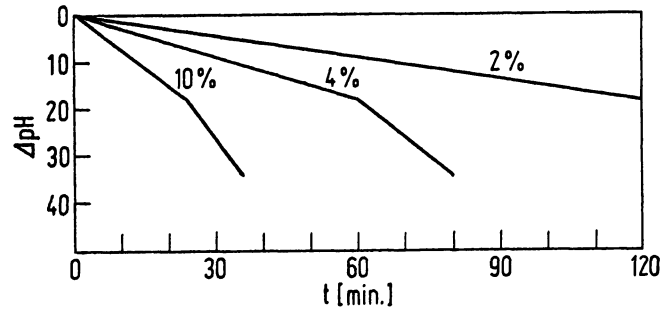

Fig. 6. Change in fetal pH with time at different levels of oxygen deficiency and a 60/40 per cent aerobic/anaerobic metabolism

in fig. 4, where the oxygen deficit was taken as 2 per cent. If we also assume initial values similar to those found by Jacobson [4] in a normal series, the changes in pH, S_{O_2}, BD_{ECF}, and P_{CO_2} with time are illustrated in fig. 5.
Fig. 6 shows the pH changes with time when there is a 2, 4, and 10 per cent oxygen deficit. The increased rate of pH drop occurs when pH has fallen 0.18 pH units, at wich time all the oxygen stores are used up.

3. Discussion

The background for the fetal acid-base changes during normal delivery has been given earlier (Jacobson and Rooth [5]). The pH fall then observed in the fetus was due to a maternal pH drop caused by **local maternal tissue hypoxia.** The pH decrease in the fetus was due to a P_{CO_2} increase and there was no significant change in fetal base deficit. The present paper gives the theoretical background for the decrease in fetal scalp blood pH during fetal oxygen deficiency. Consequently, maternal pH changes during labor

and concomitant fetal pH adjustments will be superimposed upon the pH decrease here calculated.

3.1 P_{O_2}-measurements or saturation measurements?

The clinical P_{O_2} measurements in fetal blood have usually not been considered of great value (BERG and SALING [1]). This is due partly to the S-shape of the oxygen dissociation curve. When fetal blood pH falls 0.10 units and S_{O_2} decreases from 50 to 22 per cent, then P_{O_2} drops from 22 to 15 mm Hg. **Saturation measurements therefore give a larger change in this range and also have the advantage that they directly indicate the size of the oxygen stores.**

The curves in figs. 4 and 6 give the theoretical background for the pH determination of the fetal scalp blood. Because of the strong correlation between the fall in fetal pH and oxygen saturation, the **fall in the fetal scalp pH is highly valid in itself.** However, the actual level of fetal scalp pH is so much affected by the maternal level that either the materno-fetal pH difference or the fall in the fetal pH correcting for maternal changes should be used (JACOBSON and ROOTH [5]).

If repeated scalp sampling is done and the same measurements are obtained one might be misled into thinking that the situation was unchanged. But if this were the case, both pH and oxygen saturation would have dropped according to figs. 4 and 5, the rate of fall being determined by the degree of oxygen deficiency. **Stationary values show, as just postulated, an increase in the oxygen supply to the level of the actual oxygen consumption.** Increasing pH and/or oxygen saturation values then show a further amelioration in oxygen supply, meeting the metabolic requirement and replenishing the oxygen stores.

If the fetal scalp oxygen saturation or pH are measured at known time intervals the amount of oxygen deficiency may be estimated from a series of curves of the type shown in figs. 4 or 6. **Furthermore, the survival time of the fetus may be estimated if it is assumed that death or at least serious disturbance occurs when the pH is below 7.00.**

With a 10 per cent deficit the oxygen stores are depleted after 20 minutes and pH will fall about 0.08 pH units in 10 minutes. Although this is described as occurring in about 4 per cent of the cases (SCHNEIDER [8]), the course of events usually seen when taking repeated fetal scalp samples indicates that the oxygen deficiency in most cases is of the order of 2 per cent. Moreover, stationary or low pH values are also common (SALING [7]). Thus the oxygen deficit is often only **intermittent.**

4. Optimistic conclusions

Only a small improvement in the intra-uterine gas exchange might safeguard the survival of a potentially threatened fetus. It should be investigated whether this may be reflected in the emergence, with continuous fetal heart monitoring, of a benign pattern.

The curves also demonstrate that **oxygen stores disappear much faster than glycogen.** A decrease in pH therefore always indicates a notable decrease in the margin of safety for the fetus, and when **pH has dropped about 0.20 pH units the oxygen stores have been more or less consumed.**

It follows from figs. 2 and 3 that in term infants with normal glycogen stores the total anaerobic energy stores are **not a limiting factor for survival.** Much before even half of the glycogen reserves are used up, pH will have fallen below 7.00 and the fetus will die. With **placental insufficiency or prematurity the glycogen stores are smaller,** but the rate of fall of the pH will be the same. If in these cases the cardiac glycogen stores are depleted, the heart will stop before pH has dropped to the lowest values compatible with life.

Summary

Fetal scalp blood pH is influenced by two factors, the **pH level of the mother and the oxygen supply of the fetus.** A theoretical model for the interrelation between the maternal and fetal acidbase parameters has been presented earlier. The present work concerns the theoretical background for the fetal pH drop when the fetal oxygen supply is deficient.

The fetal energy requirement during oxygen deficiency may be met either by using the oxygen stores, **i. e.** mainly the **oxygen in the hemoglobin,** or the **glycogen stores**

when lactic acid is produced during anaerobic metabolism. Curves are presented (fig. 1) showing the rate of change in the fetal oxygen saturation when the lack of oxygen is assumed to be compensated for by the oxygen stores.
Secondly, curves are given showing the base deficit increase and the pH fall when all of the oxygen deficit is balanced by anaerobic metabolism (figs. 2 to 3).
In fetal distress, some **60 per cent of the oxygen lack is supplied from the oxygen stores** and **the rest is compensated for by anaerobic metabolism** as demonstrated in a group of patients. Based upon these data, the calculated pH, P_{CO_2}, base deficit and oxygen saturation curves at 2 per cent oxygen deficit are shown (figs. 4 to 5). The pH changes during 2, 4, and 10 per cent oxygen lack are also presented (fig. 6). By comparing the clinical course with these theoretical calculations, we find that the fetal oxygen deficiency usually is only of the order of 2 per cent and only in acute, relatively rare instances, is it as high as 10 per cent.
If we use two pH measurements at a known interval **the time factor may be read off these calculated curves and should be of guidance in clinical obstetrics.** The calculations also show that a constant pH signifies adequate oxygen supply per time unit, but the lower the fetal pH, and consequently also lower fetal oxygen saturation, the smaller the margin of safety.
The small oxygen deficit usually encountered indicates that small changes in the clinical management of labor may ordinarily suffice to achieve the needed improvement in the oxygen supply.

Keywords: Fetus, acid-base status, fetal distress, oxygen, oxygen-saturation, oxygen-deficit.

Zusammenfassung

Der Zeitfaktor bei der fetalen Sauerstoffmangelversorgung
Der pH-Wert des fetalen Blutes wird von zwei Faktoren, dem **pH-Wert des mütterlichen Blutes und der Sauerstoffversorgung des Feten,** beeinflußt. Es wurde schon früher ein theoretisches Modell für die Wechselbeziehungen zwischen den mütterlichen und fetalen Parametern des Säure-Basen-Haushalts vorgelegt. Die jetzige Arbeit schlägt eine theoretische Berechnung für den Abfall des pH-Wertes des fetalen Blutes bei unzureichender Sauerstoffversorgung des Feten vor.
Das Energiebedürfnis des Feten während einer Sauerstoffmangelversorgung kann durch Ausnutzung der Sauerstoff-Speicher, hauptsächlich des **Sauerstoffs im Hämoglobin** oder der **Glykogen-Speicher** mit Hilfe von Laktatbildung im anaeroben Stoffwechsel gedeckt werden. **Abb. 1** zeigt die Veränderungen der O_2-Sättigung, wenn der Sauerstoffmangel vollständig aus dem Sauerstoff-Speicher kompensiert wird. In **Abb. 2 und 3** wird der Anstieg des Basendefizits und der Abfall der pH-Werte dargestellt, wenn der ganze Sauerstoffmangel durch anaeroben Stoffwechsel ausgeglichen wird.
An einer Gruppe von Patienten wird gezeigt, daß bei einer fetalen Sauerstoffminderversorgung **etwa 60% des Sauerstoffmangels durch die Sauerstoff-Speicher und der Rest durch anaeroben Stoffwechsel** ausgeglichen wird. Aufgrund dieser Angaben werden pH, P_{CO_2}, Basendefizit und O_2-Sättigung bei 2%igem Sauerstoffmangel geschätzt **(Abb. 4, 5).** In **Abb. 6** werden die pH-Wert-Änderungen bei 2, 4 und 10%igem Sauerstoff-Mangel gezeigt. Der Vergleich der klinischen Verläufe mit diesen theoretischen Berechnungen legt nahe, daß der fetale Sauerstoffmangel gewöhnlich in der Größenordnung von 2% und nur in akuten, relativ seltenen Fällen etwa 10% ist.
Mit Hilfe von pH-Messungen in bekannten Abständen kann man **von diesen kalkulierten Kurven den Zeitfaktor ablesen.** Er sollte eine **Orientierungsgröße für die klinische Geburtshilfe** sein. Die Schätzungen demonstrieren auch, daß ein konstanter pH-Wert eine gleichbleibende O_2-Sättigung während dieser Zeit angibt. Je tiefer jedoch der fetale pH-Wert ist, je tiefer damit also die fetale O_2-Sättigung ist, desto schmaler ist der Sicherheitsspielraum.
Bei dem gewöhnlich festzustellenden geringen Sauerstoffmangel genügen geringe Änderungen in der klinischen Geburtsleitung, um die benötigte Verbesserung in der O_2-Versorgung zu erreichen.

Schlüsselwörter: Fetus, Säure-Basen-Haushalt, Sauerstoff, Sauerstoffsättigung, Sauerstoffmangel, Asphyxie - intrauterine.

Résumé

Influence du temps (time-factor) en cas de souffrance foetale
Le pH sanguin au niveau du scalp foetal est influencé par deux facteurs: **le pH maternel et l'oxygénation foetale.**
Un schéma théorique des rapports entre l'équilibre acide-base de la mère et celui de l'enfant a déjà été publié. Le but du présent travail concerne les aspects théoriques de la chute du pH foetal lorsque l'oxygène vient à manquer.
En cas d'oxygénation insuffisante, les besoins énergétiques foetaux peuvent être couverts soit par les réserves en oxygène, c'est-à-dire essentiellement **l'oxygène lié à l'hémoglobine,** soit par les **réserves en glycogène** dont le métabolisme anaérobie produit de l'acide lactiuqe.
Des diagrammes ont été établis qui montrent, d'abord l'évolution de la saturation du sang en oxygène lorsque le déficit est compensé par les réserves oxyhémoglobinique

(fig. 1); et ensuite l'accentuation du déficit en base et la chute du pH lorsque c'est le métabolisme anaérobie du glycogène qui entre en jeu (fig. 2 et 3).
Des études faites sur un groupe de patientes montrent qu'en cas de souffrance foetale, **60% environ de la dette en oxygène est compensée par les réserves et le reste par le métabolisme anaérobie.**
Sur ces données, il est possible, par le calcul, d'établir des courbes décrivant l'évolution dans le temps du pH foetal, de la P_{CO_2} du déficit en base, et de la saturation en O_9 pour un déficit d'apport oxygéné de 2% (fig. 4 et 5). Les courbes montrant les variations du pH foetal pour des déficits en O_8 de 2, 4 et 10% ont également été établies (fig. 6).
En comparant les données cliniques à ces résultats théoriques, on peut démontrer que le déficit en oxygène est habituellement de l'ordre de 2%, et qu'il n'atteint 10% que dans de rares cas aigus.
Deux mesures du pH foetal, si elles sont séparées par un intervalle de temps connu, peuvent être reportées sur ces courbes. Elles permettent alors de mieux apprécier l'évolution (c'est-à-dire le role du temps: TIME-FACTOR), ce qui serait d'un **grand intérêt en pratique courante.**
Les calculs montrent ainsi qu'un pH constant signifie un bon apport d'oxygène par unité de temps. Mais plus le pH est bas, plus la saturation en oxygène est faible et plus la marge de sécurité réduite.
Le fait que l'on ne rencontre habituellement qu'un petit déficit en oxygène signifie que quelques moyens simples doivent suffire, le plus souvent, à rétablir au cours du travail une oxygénation foetale satisfaisante.

Mots-clés: Foetus, souffrance foetale, oxygène (saturation en, deficit en), équilibre acide-base.

Acknowledgment

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